Marine-Lenhart Syndrome

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Graves' disease and toxic nodular goiter both cause thyrotoxicosis by different pathophysiological mechanisms. Cases with both etiologies have the diagnosis of Marine-Lenhart syndrome. Such a case is presented in this paper.

Key words: Marine-Lenhart syndrome ■ Graves' disease ■ toxic nodular goiter

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INTRODUCTION

Graves' disease is thought to be caused by an autoimmune process in which stimulatory autoantibodies bind to TSH receptor and activate gland function, leading to hyperthyroidism. Thyroid nodules accompany Graves' disease in changing rates between 25% to 30% of patients according to previous reports.[1-3] A high percentage of these nodules are hypoactive according to thyroid scans (more than 95%), and a small percentage of these subjects have hyperactive nodules. Thus, these subjects have thyrotoxicosis secondary to both Graves' disease and toxic nodular goiter. These occasional patients have what is called Marine-Lenhart syndrome. A case of Marine-Lenhart syndrome, has been presented and therapeutic approach to these subjects have been discussed.

CASE REPORT

A 49-year-old woman was referred to our hospital with dizziness, palpitation and tremor in her hands. She had the same complaints 1.5 years ago. She was referred to an endocrinologist, and oral antithyroid (propylthiouracil) therapy was commenced. With a diagnosis of Graves' disease, she used the drug for one year. At the end of one year, when her thyroid hormone levels were normalized, propylthiouracil therapy was stopped. Six months later, the same symptoms appeared, and she was referred to our hospital. Her medical history showed that she had hypertension for 10 years, which was well regulated with 10 mg of oral fosinopril sodium. On laboratory examination, her thyroid hormone levels were elevated [fT3: 9 (2.2–5.4) pmol/L, fT4: 33 (9–24) pmol/L] and TSH was suppressed [0.004 (0.49–4.67) mIU/L]. Her antithyroglobulin antibodies were negative, and anti-TPO and TSH receptor antibodies (DYNOtest-Trak human; BRAHMS Diagnostika, Berlin, Germany) were positive [140 (0–60) IU/mL and 26 (0–10) U/L, respectively]. On thyroid ultrasonography, the right lobe of the thyroid was 20 x 25 x 55 mm and the left lobe was 20 x 24 x 55 mm in diameter. Solid nodules were noted on the middle of the right lobe with a diameter of 10 x 10 x 11 mm, on the superomedial aspect of the left lobe with

a diameter of 4 x 4 x 5 mm, on the middle of the left lobe with a diameter of 16 x 14 x 13 mm (Figure 1) and a cystic nodule on the inferomedial aspect of the left lobe with a diameter of 10 x 10 x 8 mm. On technetium-99 m thyroid scan, increased homogenous uptake was noted diffusely in the gland with areas of intense focal uptake, especially in the middle of the right and left lobes corresponding to the ultrasonographically detected nodules (Figure 2). The patient was initially treated with propylthiouracil for a few weeks. After achievement of euthyroidism, left total and right subtotal thyroidectomy was performed. Pathological examination revealed the previously defined nodules by ultrasound.

DISCUSSION

Graves' disease and accompanying functioning nodules are known as Marine-Lenhart syndrome.[4,5] The syndrome is rare, and prevalence was reported between 2.7% to 4.1% previously.[6,7]

When considered from the pathophysiological point of view, toxic thyroid nodules have been shown to be of clonal origin. Activating thyrotropin (TSH) receptor mutations have been found in toxic adenomas and in hot nodules contained in toxic multinodular goiter. Activity in toxic thyroid nodules may be even further enhanced by external stimulators, such as TSH or TSH receptor antibodies. In a study by Poertl et al., toxic thyroid nodules' basal hormone-releasing activities were stimulated by 15 out of 20 (75%) Graves' sera tested in vitro.[8] Thus, the existence of stimulating autoantibodies in patients with Graves' disease may play a role in the development of rare Marine-Lenhart syndrome.

On the other hand, some patients with toxic multinodular goiter may be positive for thyroid autoantibodies. Differential diagnosis between these patients and Marine-Lenhart syndrome is based on the appearance of thyroid scan. In patients with toxic multinodular goiter, increased uptake is seen on the sonographically defined areas of nodules, and the rest of the gland is suppressed. However, in Marine-Lenhart syndrome, there is diffuse increased uptake in the gland with focuses of enhancement on the sonographically defined areas of nodules.

Patients with Graves' disease should be evaluated for the existence of nodules and the functional status of them for achievement of optimal therapy. If oral antithyroid therapy is chosen as first-line treatment for Graves' disease, missed active nodules may result in the failure of achievement of euthyroidism. Secondly, if radioactive iodine therapy is chosen for treatment of Graves' disease, especially at centers where thyroid uptake cannot be measured, the given radioiodine doses may not be enough due to high activity of toxic nodules. There is a case in the literature reporting a case with Marine-Lenhart syndrome that had a solitary nodule and was cured with oral antithyroid therapy.[9] This response was interpreted by the authors as a change in the nature of the nodule from hot to cool along with the antithyroid treatment. This may be true for occasional cases with solitary nodules (toxic adenomas). However, when multiple nodules exist, surgical intervention may be more appropriate for these patients as these subjects require higher doses of radioactive iodine for successful treatment, and cure with oral antithyroid therapy is not expected when considered from the pathophysiological point of view. Surgical approach was also the treatment of choice for our case as she

Figure 1. Ultrasonographic appearance of the dominant nodule.

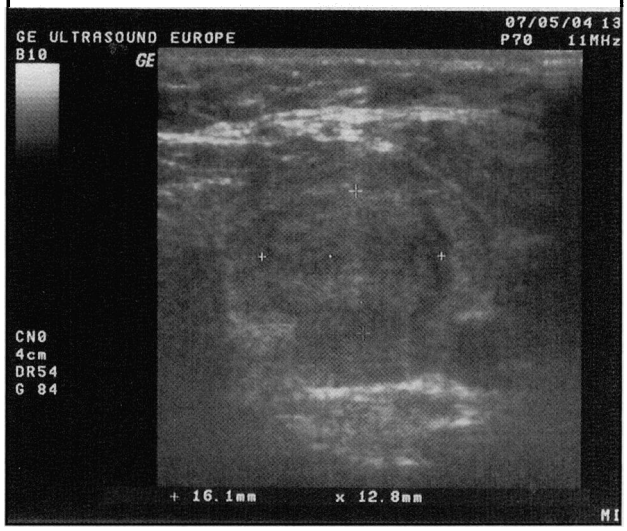
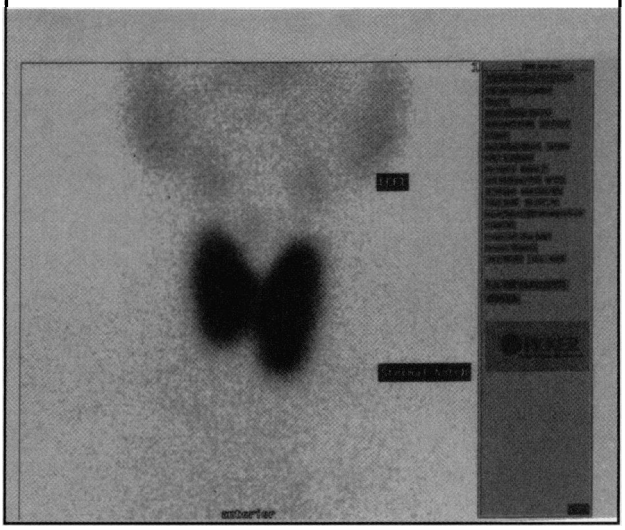


Figure 2. Technetium-99m thyroid scan of the patient, showing diffusely increased uptake with intense focal uptake areas in the middle of right and left lobes corresponding to the ultrasonographically detected nodules.



had multiple nodules.

As a conclusion, physicians must be careful in interpreting thyroid scans in Graves' disease. If treatment of thyrotoxicosis requires high doses of oral antithyroid therapy or relapse occurs soon after oral antithyroid therapy is stopped, this should alert the physician about existence of toxic nodules, thus Marine-Lenhart syndrome. After the existence of thyroid nodules are carefully evaluated, their activity status should be taken into consideration for optimal choice of treatment.

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